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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/693,794	10/23/2003	Jerome B. Zeldis	9516-076-999	2021

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EXAMINER	
OLSON, ERIC	
ART UNIT	PAPER NUMBER
1623	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/12/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/693,794	ZELDIS ET AL.	
	Examiner	Art Unit	
	Eric S. Olson	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,9,23 and 27-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5, 9, 23, and 27-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

This office action is a response to applicant's communication submitted March 8, 2007 wherein claims 1, 2, 9, and 23 are amended, claims 6, 8, 15, and 16 are cancelled, and new claims 27-34 are introduced. This application claims priority to provisional application 60/421003, filed October 24, 2002.

Claims 1-5, 9, 23, and 27-34 are pending in this application.

Claims 1-5, 9, 23, and 27-34 as amended are examined on the merits herein.

Applicant's amendment, submitted March 8, 2007, with respect to the rejection of instant claims 1-6, 8-9, 15, 16, and 23 under 35 USC 112, first paragraph, for lacking enablement for a method of preventing or modifying pain, or administering a prophylactically effective amount of a second active agent, has been fully considered and found to be sufficient to remove the rejection as the claims as amended are drawn solely to a method of treating a disorder. Therefore the rejection is withdrawn.

Applicant's amendment, submitted March 8, 2007, with respect to the rejection of instant claims 1-6, 8-9, and 23 under 35 USC 112, first paragraph, for lacking enablement for a method involving any cytokine inhibitory drug whatsoever, has been fully considered and found to be sufficient to remove the rejection as the claims as amended are drawn to a method involving a specific drug that is enabled by the specification. Therefore the rejection is withdrawn.

Applicant's amendment, submitted March 8, 2007, with respect to the rejection of instant claims 1, 6, 8, and 9 under 35 USC 102(b), for being anticipated by Rajkumar et al., has been fully considered and found to be sufficient to remove the rejection as the claims as amended are drawn to a method involving a specific drug that is not thalidomide. Therefore the rejection is withdrawn.

Applicant's amendment, submitted March 12, 2007, with respect to the rejection of instant claims 1, 6, and 15 under 35 USC 102(e), for being anticipated by Olmarker et al., has been fully considered and found to be sufficient to remove the rejection as the claims as amended are drawn to a method of treating complex regional pain syndrome, which is not a nerve root injury. Therefore the rejection is withdrawn.

Applicant's amendment, submitted March 12, 2007, with respect to the rejection of instant claims 2-5 and 23 under 35 USC 103, for being obvious over Rajkumar et al. in view of Merck, has been fully considered and found to be sufficient to remove the rejection as the claims as amended are drawn to a method involving a specific drug that is not thalidomide. Therefore the rejection is withdrawn.

Applicant's amendment, submitted March 12, 2007, with respect to the rejection of instant claims 2-5 and 23 under 35 USC 103, for being obvious over Olmarker et al. in view of Merck, has been fully considered and found to be sufficient to remove the

rejection as the claims as amended are drawn to a method of treating complex regional pain syndrome, which is not a nerve root injury. Therefore the rejection is withdrawn.

Applicant's amendment, submitted March 12, 2007, with respect to the rejection of instant claim 16 under 35 USC 103, for being obvious over Olmarker et al. in view of Remington, has been fully considered and found to be sufficient to remove the rejection as the claims as amended are drawn to a method of treating complex regional pain syndrome, which is not a nerve root injury. Therefore the rejection is withdrawn.

Applicant's amendment, submitted March 12, 2007, with respect to the rejection of instant claims 1, 6, and 16 under the doctrine of obviousness-type double patenting, for claiming the same invention as claims 1 and 4 of US patent 5635517 or 1, 5, 9, 22, and 23 of 5955476, in view of claims 1, 21, and 27 of US patent 6635250, has been fully considered and found to be sufficient to remove the rejection as the claims as amended are drawn to a method of treating complex regional pain syndrome, which is not a nerve root injury. Therefore the rejection is withdrawn.

Applicant's amendment, submitted March 12, 2007, with respect to the rejection of instant claims 1, and 6 under the doctrine of obviousness-type double patenting, for claiming the same invention as Claim 17 of 6020358, Claim 15 of 6011050, Claim 7 of 5798368, Claim 31 of 5698579, Claims 1-12 of 5736570, Claims 14-15 of 5703098, Claim 12 of 6395754, Claim 10 of 6180644, Claims 7 and 9 of 6130226, Claim 6 of

6075041, Claims 1-2 of 6214857, or Claims 8 and 11 of 5968945, has been fully considered and found to be sufficient to remove the rejection as the claims as amended are drawn to a method using a specific therapeutic agent that is not claimed by these patents. Therefore the rejection is withdrawn.

The following new grounds of rejection are introduced:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 9, 27-30, and 33-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Omoigui (US patent publication 20040038874, cited in PTO-1449) in view of Olmarker et al. (PCT international publication WO02080891, of record in previous office action) Omoigui discloses a method for the treatment of persistent pain by administering a drug that antagonizes one or more mediators of inflammation. (p. 1, paragraph 0004) Drugs useful in this manner include TNF-α blockers, (p. 2, paragraphs 0007 and 0011) including thalidomide and analogues as a specific embodiment. (p. 3, paragraph 0023) Reflex Sympathetic Dystrophy, otherwise known as chronic regional pain syndrome, is listed as a disease treatable by this method. (pp. 9-10, paragraphs 0078-0082) Omoigui does not disclose a method using the specific compounds of the

claimed invention in the specific dosage amounts listed, in the dosage forms of instant claims 27-30 and 33-34.

Olmarker et al. discloses a method of treating low back pain due to leakage of the nucleus pulposus from a damaged intravertebral disk, comprising administering a TNF inhibitor. (pp. 4-6) Because the mechanism of this pain involves the irritation of an affected nerve, it is considered to be a form of neuropathic pain. Specific compounds useful in the method of Olmarker et al. include thalidomide derivatives, including the compound CDC-501, which according to its chemical abstracts registry entry, is identical to the immunomodulatory compound 3-(4-amino-1-oxo-1,3-dihydro-isoindol-2-yl)-piperidine-2,6-dione used in the claimed method. (p. 7, lines 24-26) The compound can be administered orally as a pill, syrup, or lozenge, (p. 9, lines 11-12) in an oral dose of 10-300 mg. (p. 9, line 20) The compounds can be administered in combination with other active agents. (p. 12, lines 4-7)

It would have been obvious to one of ordinary skill in the art at the time of the invention to practice the therapeutic method of Omoigui using the compound 3-(4-amino-1-oxo-1,3-dihydro-isoindol-2-yl)-piperidine-2,6-dione in the specific dosage amounts listed, in the dosage forms of instant claims 27-30 and 33-34. One of ordinary skill in the art would have been motivated to practice the invention in this manner because Olmarker et al. discloses that the claimed compound is a TNF-α inhibitor and a thalidomide analog, and thus useful in the method of Olmarker. One of ordinary skill in the art would have been motivated to administer the compound orally and in combination with other active agents because these limitations are taught by Olmarker

for this compound. One of ordinary skill in the art would have been motivated to administer a dosage of 5-50 mg because this dosage range overlaps substantially with the dosage range of 10-300 mg taught by Olmarker et al. One of ordinary skill in the art would have been motivated to administer the compound as a tablet or capsule because these dosage forms are similar to the pill and lozenge oral dosage forms taught by Olmarker. One of ordinary skill in the art would have been motivated to administer the compounds as a pharmaceutically acceptable salt, solvate, or stereoisomer because these pharmaceutically acceptable dosage forms are routine and well known in the art for compounds to be administered as pharmaceuticals. One of ordinary skill in the art would have reasonably expected success in using this specific compound because Olmarker et al. already discloses that the compound can be used to treat other TNF-dependant pain syndromes such as lower back pain. One of ordinary skill in the art would have reasonably expected success in using the specific claimed dosage form and amounts because determining the exact details of the dosage form to be administered is well within the ordinary and routine level of skill in the art.

Thus the invention taken as a whole is *prima facie* obvious.

Claims 2-5 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Omoigui (US patent publication 20040038874, cited in PTO-1449) in view of Olmarker et al. (PCT international publication WO02080891, of record in previous office action) in view of the Merck manual of diagnosis and therapy, seventeenth edition. (Herein referred to as Merck, of record in previous office action)

The disclosure of Omoigui in view of Olmarker et al. is discussed above. Omoigui in view of Olmarker et al. does not disclose a method further comprising administering the additional therapeutic agents of instant claims 2-5 or the therapies of instant claim 23.

Merck discloses that complex regional pain syndrome may be treated with several drugs including nifedipine, prednisone, opioid analgesics, tricyclic antidepressants, and anticonvulsants. (p. 1373, left column, second paragraph) It should be noted that it is well known in the art that opioid analgesics include oxycodone, tricyclic antidepressants include amitryptyline, imipramine, and doxepin, and anticonvulsants include gabapentin. Merck also discloses that physical therapy is essential throughout therapy for complex regional pain syndrome (p. 1373, left column, last paragraph) and that pain relief that outlasts the administration of a sympathetic block but is still transitory suggests the need for surgery. (p. 1373, left column, second paragraph)

It would have been obvious to one of ordinary skill in the art at the time of the invention to practice the method of Omoigui for the treatment of complex regional pain syndrome further comprising administering one or more of the pharmaceutical active agents described by Merck and still further administering physical therapy and/or surgery. One of ordinary skill in the art would have been motivated to combine these teachings because Omoigui and Merck both disclose their respective teaching as being useful for treating the same condition, namely complex regional pain syndrome. One of ordinary skill in the art would reasonably have expected success because combining

two treatments known in the prior art to be effective for treating the same disorder by different methods is reasonably expected to produce at least additive effects.

Thus the invention taken as a whole is *prima facie* obvious.

Claims 31 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Omoigui (US patent publication 20040038874, cited in PTO-1449) in view of Olmarker et al. (PCT international publication WO02080891, of record in previous office action) in view of Remington. (of record in previous office action)

The disclosure of Omoigui in view of Olmarker et al. is discussed above. Olmarker et al. does not disclose a method comprising administering the therapeutic compound in an enantiomerically pure form.

Remington discloses that different enantiomers of the same compound may possess different biological and pharmacological activities. (pp. 462-463)

It would have been obvious to one of ordinary skill in the art at the time of the invention to practice the invention of Omoigui in view of Olmarker using enantiomerically pure 3-(4-amino-1-oxo-1,3-dihydro-isoindol-2-yl)-piperidine-2,6-dione. One of ordinary skill in the art would have been motivated to practice the invention in this manner because, as Remington discloses that the two enantiomers of a chiral compound possess different activities *in vivo*, it stands to reason that one of the two enantiomers of 3-(4-amino-1-oxo-1,3-dihydro-isoindol-2-yl)-piperidine-2,6-dione possesses better activity and/or reduced side effects compared to the other enantiomer, and is thus a better drug in its enantiomerically pure form. One of ordinary skill in the art would

reasonably have expected success because testing two enantiomers for a known activity to determine which is the best drug candidate is a small and routine experimental burden well within the ordinary level of skill in the art.

Thus the invention taken as a whole is *prima facie* obvious.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 6, and 15 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over either claims 1 and 4 of U.S. Patent No. 5635517 (Reference cited in PTO-1449, herein referred to as '517) or alternately claims 1, 5, 9, 22, and 23 of U.S. Patent No. 5955476 (Reference of record in previous office action, herein referred to as '476) in view of Omoigui (US patent publication

20040038874, of record in previous office action) Claims 1 and 4 of '517 and claims 1, 5, 9, 22, and 23 of '476 are drawn to methods of reducing undesirable levels of TNF-α in a mammal by administering the same compound recited in the instant claims. Said claims do not disclose a method of treating complex regional pain syndrome in this manner.

Omoigui discloses a method for the treatment of persistent pain by administering a drug that antagonizes one or more mediators of inflammation. (p. 1, paragraph 0004) Drugs useful in this manner include TNF-α blockers, (p. 2, paragraphs 0007 and 0011) including thalidomide and analogues as a specific embodiment. (p. 3, paragraph 0023) Reflex Sympathetic Dystrophy, otherwise known as chronic regional pain syndrome, is listed as a disease treatable by this method. (pp. 9-10, paragraphs 0078-0082)

It would have been obvious to one of ordinary skill in the art at the time of the invention to practice the methods of claims 1 and 4 of '517 and claims 1, 5, 9, 22, and 23 of '476 on a mammal suffering from neuropathic pain caused by a herniated disk. One of ordinary skill in the art would have been motivated to practice the invention in this manner because claims 1, 21, and 27 of '250 disclose that blocking the action of TNF-α is an effective strategy for treating neuropathic pain in a herniated disk. One of ordinary skill in the art would have reasonably expected success because claims 1, 21, and 27 of '250 already demonstrate the utility of this method.

Summary

No claims are allowed in this application.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eric S. Olson whose telephone number is 571-272-9051. The examiner can normally be reached on Monday-Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on (571)272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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